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| 10/652,864 | 08/29/2003 | Heinz Kohler | IXS-10002/49 | 1487 |

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| EXAMINER | |
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| BLANCHARD, DAVID J | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/652,864 | KOHLER ET AL. | |
| | Examiner | Art Unit | |
| | David J. Blanchard | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *7-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7,29/08; 8/20/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to the undersigned.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 20 August 2008 has been entered.

3. Claims 1-6 and 11-17 are cancelled.
Claims 7-10 have been amended.

4. Claims 7-10 are under consideration.

5. This Office Action contains New Grounds of Rejections.

### *Information Disclosure Statement*

6. The information disclosure statement (IDS) submitted on 20 August 2008 has been fully considered by the examiner. A signed and initialed copy of the IDS is included with the instant Office Action. It is noted that the reference listed on the IDS submitted 29 July 2008 are duplicate citations of the IDS submitted 20 August 2008 and as such have been crossed out on the IDS filed 29 July 2008. Applicants' cooperation is requested in avoiding duplicate citations that will result in delays at the time of issue. For clarity of the record, all of the references listed on the IDS filed 29 July 2008 are also listed on the IDS filed 20 August 2008 and have been fully considered by the examiner.

***New Grounds of Rejections***

**Claim Rejections - 35 USC § 103**

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura et al (Cancer Research, 54(6):1511-1516, 1994) in view of Kohler et al [a] (U.S Patent 6,238,667, filed 5/4/1998, IDS reference filed 9/23/04) and Kang et al (Science, 240:1034-1036, 1988, IDS reference filed 11/7/05).

The applied reference (Kohler et al [a]) has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it

constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Nakamura et al teach a chimeric antibody (KM966) specific for ganglioside GM2 expressed on the cell surface of human tumors of neuroectodermal origin, wherein KM966 markedly suppressed the establishment of human tumors and showed strong antitumor activity both in vitro and in vivo and Nakamura et al suggest KM966 as a useful agent for immunotherapy of human cancer (see entire document). Nakamura et al do not specifically teach a method of producing a KM966 autophilic antibody by chemical techniques, wherein the T15 autophilic peptide comprising SEQ ID NO:1 is photo-crosslinked to a nucleotide affinity site of the KM966 antibody. This deficiency is made up for in the teachings of Kohler et al [a] and Kang et al.

Kohler et al [a] teach methods of producing an autophilic antibody using mild photo-reactive chemistry, wherein an is antibody conjugated to a biologically active peptide via a nucleotide affinity site of the antibody, wherein the biologically active peptide includes signal peptides (i.e., membrane transport), antigenic peptides (i.e., immunostimulatory) and peptides from the selfbinding locus of antibodies (i.e., homophilic) (see col. 6, lines 35-38) and Kohler [a] teaches that the selfbinding or homophilic peptides increase the valency and overall avidity for the antigen (see entire document, particularly abstract, cols. 1-7 and claims).

Kang et al teach a 24 residue peptide (T15 peptide; conserved selfbinding sequence) in the heavy chain of the idiotypic antibody T15 that is responsible for self-binding and dimeric T15 binds more strongly than monomeric T15 (see entire document, particularly pg. 1034).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method of producing chimeric anti-GM2 antibody KM966 crosslinked to the autophilic peptide T15 comprising SEQ ID NO:1 via a nucleotide affinity site using mild photo-reactive chemistry according to Kohler et al [a] for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated and would have reasonable expectation of success to have produced a method of producing the anti-GM2 antibody KM966 crosslinked to the autophilic peptide T15 comprising SEQ ID NO:1 via a nucleotide affinity site using mild photo-reactive chemistry according to Kohler et al [a] for therapeutic benefit in human cancer patients in view of Nakamura et al and Kohler et al [a] and Kang et al because Nakamura et al teach a chimeric antibody (KM966) specific for ganglioside GM2 expressed on the cell surface of human tumors of neuroectodermal origin, wherein KM966 markedly suppressed the establishment of human tumors and showed strong antitumor activity both in vitro and in vivo and Nakamura et al suggest KM966 as a useful agent for immunotherapy of human cancer and Kohler et al [a] teach methods of producing an autophilic antibody using mild photo-reactive chemistry, wherein an is antibody conjugated to a biologically active peptide via a nucleotide affinity site of the antibody, wherein the biologically active peptide includes signal peptides (i.e., membrane transport), antigenic peptides (i.e., immunostimulatory) and peptides from the selfbinding locus of antibodies (i.e., homophilic) and Kohler [a] teaches that the selfbinding or homophilic peptides increase the valency and overall avidity for the antigen and Kang et al teach a 24 residue peptide (T15 peptide) in the heavy chain of the idiotypic antibody T15 that is responsible for selfbinding and dimeric T15 binds more strongly than monomeric T15. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to modify the anti-GM2 KM966 antibody of Nakamura et al by conjugating KM966 to the homophilic or self-

binding T15 peptide of Kang et al using the mild-photo-reactive chemistry of Kohler et al [a] in order to produce dimeric KM966 antibodies having increased valency and avidity for GM2 in human cancer patients. Thus, there would have been an advantage to using the self-binding T15 peptide for increasing the avidity of the KM966 antibody in human cancer patients. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). See also *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a method of producing the anti-GM2 antibody KM966 crosslinked to the autophilic peptide T15 comprising SEQ ID NO:1 via a nucleotide affinity site using mild photo-reactive chemistry for therapeutic benefit in human cancer patients in view of Nakamura et al and Kohler et al [a] and Kang et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

9. Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura et al (Cancer Research, 54(6):1511-1516, 1994) in view of Kohler et al [b] (US 2003/0103984 A1, filed 5/29/2001, IDS reference filed 9/23/04) and Kang et al (Science, 240:1034-1036, 1988, IDS reference filed 11/7/05) and Zhao et al (J. Immunol. Methods, 254(1-2):137-145, August 1, 2001, IDS reference filed 11/7/05) and Singh et al (U.S. Patent 7,041,459; filed 5/21/2002, cited on PTO-892 mailed 5/125/07).

The applied reference (Kohler et al [b]) has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed

but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Nakamura et al have been described supra. Nakamura et al do not specifically teach a method of producing a KM966 autophilic antibody by chemical or genetic engineering techniques, wherein the KM966 antibody is conjugated to the T15 autophilic peptide comprising SEQ ID NO:1, wherein the T15 autophilic peptide is photo-crosslinked to a carbohydrate site of the Fc portion, or crosslinked to an amino or sulfhydryl group of the antibody, or is expressed as a fusion protein containing the T15 autophilic sequence. These deficiencies are made up for in the teachings of Kohler et al [b] and Kang et al and Zhao et al and Singh et al.

Kohler et al [b] teach methods of producing an antibody fusion protein comprising an antibody and a biologically active peptide, wherein the antibody is expressed as a fusion protein containing the biologically active peptide, wherein the biologically active peptide includes signal peptides (i.e., membrane transport), antigenic peptides (i.e., immunostimulatory) and peptides from the selfbinding locus of antibodies (i.e., homophilic) (e.g., see par. 0011-0013 and 0031) and Kohler [b] teaches that selfbinding or homophilic peptides increase the valency and overall avidity for the antigen (see entire document, particularly pp. 1-3 and par. 0005).

Kang et al have been described supra.

Zhao et al teach that linking an MTS (membrane transporting sequence) peptide sequence to a monoclonal antibody allows the monoclonal antibody to penetrate the

cellular membrane of living cells without affecting cell viability wherein attachment is via the carbohydrate moiety in the Fc domain and does not interfere with antigen recognition (see entire document, particularly abstract, pp. 137-138, 144-145).

Singh et al teach the attachment of peptide tags (e.g., e-tag) to an antibody using a number of different reactions including by reaction of amine groups of lysine, the free carboxylic acid groups of glutamic and aspartic acid and the sulfhydryl groups of the cysteine residues of antibodies (see entire document, particularly, cols. 25-27).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method of producing the anti-GM2 antibody KM966 conjugated to the autophilic peptide T15 comprising SEQ ID NO:1, wherein the T15 peptide is crosslinked to a carbohydrate site of the Fc of KM966, or crosslinked to an amino or sulfhydryl group of KM966, or expressed as a fusion protein containing the T15 autophilic sequence for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated and would have reasonable expectation of success at the time the invention was made to have produced a method of producing the anti-GM2 antibody KM966 conjugated to the autophilic peptide T15 comprising SEQ ID NO:1, wherein the T15 peptide is crosslinked to a carbohydrate site of the Fc of KM966, or crosslinked to an amino or sulfhydryl group of KM966, or expressed as a fusion protein containing the T15 autophilic sequence for therapeutic benefit in human cancer patients in view of Nakamura et al and Kohler et al [b] and Kang et al and Zhao et al and Singh et al because Nakamura et al teach a chimeric antibody (KM966) specific for ganglioside GM2 expressed on the cell surface of human tumors of neuroectodermal origin, wherein KM966 markedly suppressed the establishment of human tumors and showed strong antitumor activity both in vitro and in vivo and Nakamura et al suggest KM966 as a useful agent for immunotherapy of human cancer and Kohler et al [b] teach methods of producing an antibody fusion protein comprising an antibody and a biologically active peptide, wherein the antibody is expressed as a fusion protein containing the biologically active peptide, wherein the biologically active peptide includes signal peptides (i.e., membrane

transport), antigenic peptides (i.e., immunostimulatory) and peptides from the selfbinding locus of antibodies (i.e., homophilic), and Kohler [b] teaches that selfbinding or homophilic peptides increase the valency and overall avidity for the antigen and Kang et al teach a 24 residue peptide (T15 peptide) in the heavy chain of the idiotypic antibody T15 that is responsible for selfbinding and dimeric T15 binds more strongly than monomeric T15 and Zhao et al teach that linking an MTS (membrane transporting sequence) peptide sequence to a monoclonal antibody allows the monoclonal antibody to penetrate the cellular membrane of living cells without affecting cell viability wherein attachment is via the carbohydrate moiety in the Fc domain and does not interfere with antigen recognition and Singh et al teach the covalent attachment of a peptide tag to the amine group of lysine or the sulfhydryl groups of the cysteine residues in an immunoglobulin molecule. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to modify the anti-GM2 KM966 antibody of Nakamura et al by conjugating the KM966 antibody to the homophilic/self-binding T15 peptide crosslinked to the carbohydrate site of the Fc of KM966, or crosslinked to an amino or sulfhydryl group of KM966, or expressed as a KM966-T15 fusion protein in order to produce dimeric KM966 antibodies having increased valency and avidity for GM2 in human cancer patients. Thus, there would have been an advantage to using the self-binding T15 peptide for increasing the avidity of the KM966 antibody in human cancer patients. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). See also *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a method of producing the anti-GM2 antibody KM966 conjugated to the autophilic peptide T15 comprising SEQ ID NO:1, wherein the T15 peptide is crosslinked to a carbohydrate site of the Fc of KM966, or crosslinked to an amino or sulfhydryl group of KM966, or expressed as a fusion protein containing the

T15 autophilic sequence for therapeutic benefit in human cancer patients in view of Nakamura et al and Kohler et al [b] and Kang et al and Zhao et al and Singh et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

### ***Double Patenting***

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 7-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1 in view of Nakamura et al (Cancer Research, 54(6):1511-1516, 1994) and Kohler et al [b] (US 2003/0103984 A1, filed 5/29/2001, IDS reference filed 9/23/04) and Kang et al (Science, 240:1034-1036, 1988, IDS reference filed 11/7/05) and Zhao et al (J. Immunol. Methods, 254(1-2):137-145, August 1, 2001, IDS reference filed 11/7/05)

and Singh et al (U.S. Patent 7,041,459, filed 5/21/2002, cited on PTO-892 mailed 5/125/07).

Claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1 are drawn to a method of affinity cross-linking a peptide to an antibody so that the peptide becomes attached to the antibody at a location where the peptide does not compromise antigen binding, the method comprising the steps of (a) providing an antibody, the antibody having a variable domain, the variable domain including a hydrophobic structure, the hydrophobic structure defining a binding pocket having a tryptophan-binding site, and wherein the hydrophobic structure is located away from the antigen binding site that is in the Fv domain of the antibody, (b) providing a peptide that has an azido tryptophan residue, wherein said azido tryptophan residue is 5-azido tryptophan or 6-azido tryptophan, the azido tryptophan residue having an affinity for the hydrophobic structure of the variable domain of the antibody, (c) photo-chemically activating the azido tryptophan residue of the peptide, and (d) allowing the peptide and the antibody to interact whereby the photo-chemically activated azido tryptophan residue binds to the hydrophobic structure of the variable domain and reacts with the tryptophan-binding site whereby the peptide becomes cross-linked to the antibody, whereby, because the location of the hydrophobic structure is away from the antigen binding site that is in the Fv domain of the antibody, the cross-linked peptide does not compromise the antigen recognition of the antibody and wherein the peptides has a biological activity selected from immuno-stimulatory, membrane transport, homophilic and antigenic activities and the antibody is a full-length immunoglobin molecule or a variable domain fragment of an antibody. Claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1 do not specifically teach wherein the peptide is the autophilic peptide T15 comprising SEQ ID NO:1, or wherein the autophilic peptide is crosslinked to a carbohydrate site of the Fc portion, or crosslinked to an amino or sulfhydryl group of the immunoglobulin, or is expressed as a fusion protein containing the T15 autophilic sequence. These deficiencies are made up for in the teachings of Nakamura et al and Kohler et al [b] and Zhao et al and Singh et al.

Nakamura et al have been described supra.

Kohler et al [b] have been described supra.

Zhao et al have been described supra.

Singh et al have been described supra.

The claims in the instant application are obvious variants of claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a method of producing the anti-GM2 antibody KM966 conjugated to the autophilic peptide T15 comprising SEQ ID NO:1, wherein the T15 peptide is crosslinked to a nucleotide affinity site using mild photo-reactive chemistry according to claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1, or crosslinked to a carbohydrate site of the Fc of KM966, or crosslinked to an amino or sulfhydryl group of KM966, or expressed as a fusion protein containing the T15 autophilic sequence for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a method of producing the anti-GM2 antibody KM966 conjugated to the autophilic peptide T15 comprising SEQ ID NO:1, wherein the T15 peptide is crosslinked to a nucleotide affinity site using mild photo-reactive chemistry according to claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1, or crosslinked to a carbohydrate site of the Fc of KM966, or crosslinked to an amino or sulfhydryl group of KM966, or expressed as a fusion protein containing the T15 autophilic sequence for therapeutic benefit in human cancer patients in view of claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1 and Nakamura et al and Kohler et al [b] and Kang et al and Zhao et al and Singh et al because Nakamura et al teach a chimeric antibody (KM966) specific for ganglioside GM2 expressed on the cell surface of human tumors of neuroectodermal origin, wherein KM966 markedly suppressed the establishment of human tumors and showed strong antitumor activity both in vitro and in vivo and Nakamura et al suggest KM966 as a useful agent for immunotherapy of human cancer and Kohler et al [b] teach methods of producing an antibody fusion protein comprising an antibody and a

biologically active peptide, wherein the antibody is expressed as a fusion protein containing the biologically active peptide, wherein the biologically active peptide is a signal peptide (i.e., membrane transport), an antigenic peptide (i.e., immunostimulatory) or a peptide from the selfbinding locus of antibodies (i.e., homophilic) and Kohler [b] teaches that selfbinding or homophilic peptides increase the valency and overall avidity for the antigen and Kang et al teach a 24 residue peptide (T15 peptide) in the heavy chain of the idiotypic antibody T15 that is responsible for selfbinding and dimeric T15 binds more strongly than monomeric T15 and Zhao et al teach that linking an MTS (membrane transporting sequence) peptide sequence to a monoclonal antibody allows the monoclonal antibody to penetrate the cellular membrane of living cells without affecting cell viability wherein attachment is via the carbohydrate moiety in the Fc domain and does not interfere with antigen recognition and Singh et al teach the covalent attachment of a peptide tag to the amine group of lysine or the sulfhydryl groups of the cysteine residues in an immunoglobulin molecule. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to modify the anti-GM2 KM966 antibody of Nakamura et al by conjugating the KM966 antibody to the homophilic/self-binding T15 peptide crosslinked to a nucleotide affinity site using mild photo-reactive chemistry, or crosslinked to a carbohydrate site of the Fc of KM966, or crosslinked to an amino or sulfhydryl group of KM966, or expressed as a KM966-T15 fusion protein in order to produce dimeric KM966 antibodies having increased valency and avidity for GM2 in human cancer patients. Thus, there would have been an advantage to using the self-binding T15 peptide for increasing the avidity of the KM966 antibody in human cancer patients. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a method of producing the anti-GM2 antibody KM966 conjugated to the autophilic peptide T15 comprising SEQ ID NO:1, wherein the T15 peptide is crosslinked to a nucleotide affinity site using mild photo-reactive chemistry according to claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1, is crosslinked to the carbohydrate site of the Fc of KM966, is crosslinked to an amino or sulfhydryl group of KM966, or expressed as a fusion protein containing the T15 autophilic sequence for therapeutic benefit in human

cancer patients in view of claims 1-3, 7, 10-11 and 17 of U.S. Patent No. 6,238,667 B1 and Nakamura et al and Kohler et al [b] and Kang et al and Zhao et al and Singh et al.

Claims 7-10 are directed to an invention not patentably distinct from claims 1-3, 7, 10-11 and 17 of commonly assigned U.S. Patent No. 6,238,667 B1. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 6,238,667 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Blanchard/
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